

The Independence of Neurotic Depression and Endogenous Depression

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INTRODUCTION

In 1926 Mapother stated that in manic depressive psychosis we are dealing with "a merely quantitative deviation" from the normal, morbid only in its undue prolongation or if disproportionate or disastrous in its degree. He included anxiety neuroses along with mania and all varieties of depression as members of the manic depressive group. Perhaps these beliefs reflected the inevitable pessimism of a period when therapy was largely expectant and custodial. Somewhat despondently Mapother goes on to say "sub-division serves little purpose unless the types discriminated are correlated with differences in the unknown—for example in causation, prognosis and treatment".

In the 1930's there was considerable conflict between those accepting the traditional diagnostic distinctions and those who adopted Mapother's views; the arguments and counter-arguments are well summarized by Partridge (1949). It is interesting that these long and sometimes acrimonious discussions centred entirely on the problems of depression and anxiety. No one seemed prepared to follow Mapother to the logical extreme that any argument valid in the field of depression must equally be applicable to cases of mania.

Mapother's views on depression were made the basis of an M.D. thesis (1929) and of two lengthy papers by Lewis (1934; 1936) which still exert considerable influence on psychiatric thought, in spite of the fact that Mapother's "unknown" has undergone considerable contraction and correlations between the depressive syndromes and both prognosis and treatment are now possible.

Not only did Mapother consider it pointless to differentiate between a host of widely differing clinical pictures, but he found the task difficult

in practice. Certainly, differentiation may be very difficult indeed; but this is no justification for saying that distinctions do not exist. It may even be that the two broad categories of depressive illness themselves are heterogeneous and as Kraines (1957) has pointed out, endogenous depression may itself prove a source of stress and provoke further "reactive" symptoms. These symptoms in turn may vary widely in form according to the personality of the individual, so that it is indeed difficult and often impossible, to evaluate accurately the various constituents of the illness. It is not as easy in psychiatry as in other branches of medicine to differentiate an illness from its consequences. Such difficulties reflect the inadequacy of our clinical methods and the lack of objectivity in our approach and should not be construed as a criticism of the nosological aspects of these cases.

The fact that certain symptoms show a continuous distribution throughout the clinical material does not imply that the material is aetiologically homogeneous. In the cases under consideration depression is continuously distributed, for the cases were selected on this account. A material may in fact be aetiologically heterogeneous even though the clinical features are identical—class A and class B mongols, which have only recently been differentiated by elaborate cytological techniques, provide a case in point.

Many of the clinical features observed in cases suffering from depressive states must be secondary in nature, and some, as Sloane (1961) suggests, may even be of a tertiary order. In view of the relatively small range of phenomena that occurs in the affective disorders, it is hardly surprising that a considerable overlap in the clinical features should exist.

The need for an adequate system of classifi-

cation in psychiatry is not accepted by everyone as pressing, yet it is difficult to see how we can progress far without one. There is a common feeling—implicit in the writings of some of the authors already quoted—that knowledge of aetiology must precede classification. This of course is simply not true and as Cattell (1943) has pointed out forcibly, the reverse is the case—“nosology necessarily precedes aetiology”. Eysenck (1960) reiterates the same inescapable fact—“before we can reasonably be asked to look for the cause of a particular dysfunction or disorder we must have isolated, however crudely, the dysfunction or disorder in question and we must be able to recognize it and differentiate it from other syndromes”.

Semantic problems as usual have contributed to the confusion. Arguments about the validity of the concepts of neurosis and psychosis, of the meanings of such words as “endogenous”, “reactive” and “psychogenic” served to obscure the basic issue. Sometimes—a reflection of the unitary approach—the word psychotic is used as an index of the depth of depression which may be described as “of psychotic intensity”. The word “reactive” in particular has been a source of much fruitless discussion. It is often correctly pointed out that many attacks of endogenous depression are precipitated by adverse circumstances and are therefore in this sense reactive, but this does not necessarily indicate that the precipitants play an important causal role. The word “reactive” may also be employed in the sense that the depression is reactive—or responsive—to day-to-day vicissitudes.

Few of the terms we use are beyond criticism, and until aetiological factors are fully elucidated and understood it is difficult to see how a rational and acceptable terminology can be achieved. In the meantime, it is as well to make do with what we have and to cease to indulge in profitless arguments on this score.

In this paper the terms “neurotic depression” and “endogenous depression” are employed, as it is felt that these are the best of an imperfect range available. They have the advantage of being understood, even by those who profess not to accept them. There seems little point in introducing new terms to add to the confusion. An exception occurs when other authors

are quoted, their terminology usually being retained.

METHOD AND RESULTS

In the course of a double-blind controlled clinical trial of the effects of imipramine upon patients suffering from depressive states, a great deal of clinical and social data was amassed upon the patients treated (Ball and Kiloh, 1959; Kiloh and Ball, 1961). It was clear from the results that those patients diagnosed as suffering from endogenous depression made a significantly better response to the drug than those regarded as showing neurotic depression. A discriminant function analysis was carried out on the data from 97 patients all treated with imipramine, which showed that one cluster of symptoms correlated positively and a second cluster of symptoms correlated negatively with a good response to imipramine. The first cluster included items which many regard as characteristic of endogenous depression whilst the second cluster included items often accepted as features of neurotic depression. It was felt that these results suggested that endogenous and neurotic depression were distinct nosological entities (Kiloh *et al.*, 1962).

In order to test this hypothesis further it was felt desirable to carry out a factor analysis and the opportunity was taken to extend the clinical material, 46 further cases being added. These were mostly patients that one felt could be diagnosed confidently as suffering either from endogenous or from neurotic depression, using the same criteria as in the original group.

The entire material consisted therefore of 143 cases, in 92 of which the diagnosis was made with reasonable confidence (see Table I). Of a total of 60 items assessed in each patient, 35 (see

TABLE I
Distribution by Diagnosis

	Reasonably Certain	Doubtful	Total
Endogenous depression	31	22	53
Neurotic depression ...	61	29	90
Total ...	92	51	143

Table II) were selected for further study. It was necessary to reduce the number of items, owing to the limitations of the Ferranti Pegasus Computer which was used to process the data.

TABLE II
Clinical Features Selected for Analysis

Personal details

1. Age (when first seen)
2. Sex
3. Married at any time

Personality traits

4. Anxiety
5. Obsessionality
6. Reactive depression
7. Hysterical features; immaturity
8. Inadequacy

Previous history

9. Previous attacks of depression

Present illness

10. Duration
11. Mode of onset (insidious or sudden)
12. Precipitants
13. Depth of depression
14. Quality of depression
15. Reactivity of depression
16. Depression worse in early morning
17. Depression worse in evening
18. Self reproach or guilt
19. Retardation
20. Agitation (Motor restlessness)
21. Weight loss of 7 lbs. or more
22. Suicidal ideas
23. Suicidal attempt
24. Subjective anxiety
25. Phobias
26. Irritability
27. Failure of concentration
28. Hypochondriasis
29. Hysterical features
30. Self-pity
31. Paranoid features
32. Variability of illness
33. Initial insomnia
34. Restless sleep
35. Early awakening

Definitions

Most of the terms used are self explanatory. Those requiring further elucidation are dealt with below.

Duration. In the case of patients having had previous attacks, the duration of the present episode was recorded.

Mode of onset. The onset of the illness is described as sudden when it reaches its maximal or near maximal intensity within seven days. In such cases precipitants are frequently recorded. The onset is described as insidious where the evolution of the illness is slower than this.

Precipitants. Psychological disturbances clearly related to the onset of the illness and which appeared to the observer to play an important role in its genesis.

Quality of depression. Patients may describe their depression as similar to "normal" sadness or gloom, differing only in degree: others describe their experience as something beyond normal experience, having a quality distinct from "normal" depression.

Reactivity of depression. The depression is described as "reactive" (or responsive) when it responds quickly to environmental changes.

Retardation. This term is used inclusively to describe the subjective experience of slowness of thought or action and objective psychomotor slowing.

Variability of depression. The depression is described as "variable" when the mood fluctuates markedly on a day-to-day or week-to-week basis.

A score of 1 was assigned to each clinical feature when present and a score of 0 when absent, except that in the case of the following features 1 was assigned to moderate or severe and 0 assigned to absent or slight: depth of depression, reactivity of depression, agitation, subjective anxiety, failure of concentration and variability of illness. Moreover, age was scored 1 for 40 years and over and 0 for under 40 years; sex, 1 for female and 0 for male; married, 1 for married and 0 for single; duration, 1 for one year or less, 0 for over 1 year; onset, 1 for sudden, 0 for insidious; quality of depression, 1 for different from "normal" depression and 0 if the same; 1 for depression worse in morning, 0 if not; 1 for depression worse in evening, 0 if not; weight loss, 1 for 7 lbs. or more, 0 for less.

Product moment correlations were calculated between each of the 35 clinical features and a simple summation factor analysis was carried out (Burt, 1940). Two factors were extracted and the correlation was calculated between the second factor loadings and the correlation coefficients between diagnosis and each feature. These diagnosis correlations were based upon the 92 cases in which a definite diagnosis was made out of the total of 143 patients.

The intercorrelation coefficients between the features are given in Table III. The number of patients scoring 1 for each feature, the factor loadings and the correlations with diagnosis are given in Table IV. The first factor is a general factor and thus the first factor loading indicates the extent to which each feature is related to all the features as a whole, that is to depressive illness as defined by the sum of the 35 features. To

TABLE III

Intercorrelations (Decimal points omitted)

Feature	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
2	023																
3	174	-015															
4	014	139	097														
5	021	103	171	185													
6	-025	033	-041	349	257												
7	-225	060	-086	201	066	379											
8	-148	-093	-138	077	-135	235	387										
9	167	-017	094	079	-059	-043	-016	-065									
10	-069	024	-035	-191	-131	-100	007	-097	069								
11	-079	-033	-030	062	022	108	-001	084	-190	-131							
12	-124	-070	-074	-023	050	087	070	214	-234	-215	-368						
13	026	024	090	-116	-164	-152	-055	015	-029	290	-071	-169					
14	093	006	074	-064	046	-087	-294	-214	018	215	-145	-221	111				
15	-133	-047	-031	048	059	165	271	290	-100	-287	059	328	-298	-209			
16	178	060	009	027	-166	-096	-186	-189	079	100	-166	100	-166	100	-197		
17	-125	-013	-019	-149	-031	-020	046	102	-015	175	003	072	110	-104	050	-528	
18	-048	-003	-112	-193	-106	-028	037	093	167	039	-007	-135	003	010	-031	166	005
19	179	029	-026	-167	-200	-045	-126	-060	183	143	-104	-202	244	142	-221	311	-063
20	147	092	-130	027	-041	007	003	080	139	-013	052	-004	018	122	-080	106	057
21	029	-002	030	036	017	074	-183	-194	090	162	-106	-114	118	172	-186	196	-044
22	-096	-007	-047	-060	021	120	037	148	-119	009	052	034	186	-034	-095	047	-012
23	-059	053	004	-096	-177	-078	-113	-085	042	-045	064	-017	038	073	-013	049	-123
24	087	059	-150	112	-010	092	109	014	-018	-072	-177	058	-106	060	130	-058	168
25	-002	134	026	139	109	123	090	130	-013	-161	077	079	-092	-079	120	033	-041
26	-122	-029	010	-006	036	124	-050	137	-043	-106	-081	111	-059	-037	288	-104	089
27	130	093	-041	075	-049	109	097	133	073	058	014	007	137	052	-093	090	007
28	082	047	074	-028	-065	042	140	070	001	-158	-096	070	012	-099	116	-110	024
29	-123	101	-207	093	099	183	354	197	-016	-201	133	101	-133	-167	142	-183	-024
30	-045	-094	-015	-047	069	033	197	017	-083	-223	069	282	-068	-218	208	-128	-013
31	-061	-038	-004	-117	-086	-089	-001	023	030	-018	-047	-096	075	023	-016	-020	-023
32	-225	-097	-177	-087	021	042	223	148	-072	-099	-010	202	-295	-026	477	-125	149
33	-026	157	-041	133	108	144	128	031	043	-114	014	007	-093	-067	203	-201	131
34	-053	020	-031	-124	161	175	012	077	-148	-076	065	178	-003	-027	098	-120	041
35	282	-026	-021	-093	-113	-158	-294	-214	141	186	-018	-310	198	340	-507	416	-229

Feature	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
19	302																
20	227	075															
21	061	130	196														
22	184	127	218	090													
23	-009	192	049	104	257												
24	010	014	212	-086	123	045											
25	-021	-008	-026	-146	082	-040	099										
26	096	030	-031	064	120	-078	081	222									
27	173	279	149	017	309	164	117	052	125								
28	067	-112	091	-053	-073	-096	007	-099	-091	-142							
29	036	-159	171	-076	-038	-103	091	128	048	093	199						
30	130	-132	-065	-188	117	-069	059	006	326	-002	172	171					
31	197	067	052	060	075	072	-120	-123	103	071	176	062	079				
32	136	-220	077	-032	047	-063	135	004	187	-026	062	268	123	088			
33	-135	-227	119	-012	108	108	117	111	052	-057	148	191	030	-037	207		
34	124	-047	-031	087	-003	-090	-071	-027	098	-001	022	180	149	074	088	-180	
35	135	323	092	201	140	130	021	-049	-185	260	-187	-101	-250	-050	-349	-304	-178

test the hypothesis that the first factor loadings alone were sufficient to produce the original correlations between features, the statistical significance of the first factor residuals was estimated by calculating χ^2 . This is admittedly an approximate procedure when used in conjunction with a simple summation analysis, but it is probably the best method available and has empirical support (Burt, 1952). Moreover, the value of χ^2 obtained, 1415 with 560 degrees of freedom, corresponds to a unit variance normal deviate (Fisher, 1941) of 19.7. This is ten times the value usually adopted (1.96) as indicating statistical significance. Thus the hypothesis that the data are consistent with there being one

factor only is definitely disproved. The data cannot be produced by a single depressive condition, but must be produced by two separate conditions. These conditions may, of course, have some clinical features in common, as indicated by the first factor loadings, but they also differ from each other, as indicated by the bipolar second factor loadings. The sum of the squares of the first factor loadings is 1.833 and that of the second factor loadings is 3.518, and thus the second factor is more important than the first in producing the original correlations between the 35 features.

The bipolar second factor loadings in Table IV are very similar to the correlations with

TABLE IV
Numbers of Patients Showing Each Feature, Factor Loadings and Correlations with Diagnosis

Clinical feature	No. of patients showing feature, i.e., scoring 1	Factor loadings		Correlations with diagnosis
		First	Second	
1. Age 40 or above	100	-.017	-.250	-.376
2. Sex—female	102	.139	-.007	-.088
3. Married	128	-.120	-.064	-.027
4. Anxiety	68	.073	.156	.192
5. Obsessionality	42	.027	.201	.229
6. Reactive depression	31	.443	.311	.319
7. Hysterical features (immaturity)	41	.311	.409	.376
8. Inadequacy	33	.247	.315	.332
9. Previous attacks	47	.039	-.231	-.228
10. Duration 1 year or less	69	-.181	-.342	-.423
11. Sudden onset	42	-.041	.179	.286
12. Precipitation	90	.067	.476	.654
13. Depth of depression	76	.013	-.369	-.301
14. Quality of depression	53	-.027	-.389	-.523
15. Reactivity of depression	89	.179	.605	.666
16. Depression worse in morning	59	-.053	-.531	-.570
17. Depression worse in evening	44	-.062	.170	.294
18. Self reproach—guilt	45	.347	-.198	-.191
19. Retardation	52	.193	-.547	-.522
20. Agitation	59	.485	-.170	-.166
21. Weight loss 7 lbs. or more	73	.127	-.315	-.239
22. Suicidal ideas	76	.459	-.133	-.038
23. Suicidal attempt	10	.029	-.231	-.184
24. Subjective Anxiety	120	.244	.075	.082
25. Phobias	53	.178	.166	.198
26. Irritability	116	.288	.172	.261
27. Failure of concentration	87	.572	-.258	-.242
28. Hypochondriasis	82	.046	.120	.243
29. Hysterical features	38	.353	.366	.412
30. Self pity	102	.145	.322	.457
31. Paranoid features	28	.079	-.080	-.070
32. Variability of illness	59	.196	.386	.444
33. Initial insomnia	87	.178	.237	.332
34. Restless sleep	51	.095	.145	.195
35. Early awakening	53	-.065	-.692	-.831

diagnosis. The correlation between these two sets of figures is in fact .986. This is very high, particularly as no rotation was carried out. Thus the bipolar second factor differentiates between neurotic and endogenous depression. No further factor was extracted; such a factor, even if significant, would be superfluous to the present issue.

The clinical features which correlate significantly ($P < .05$) with diagnosis are listed in Table V. The features are given in order of the magnitude of their correlations with diagnosis and according to the diagnosis suggested by the presence of each feature.

TABLE V
Clinical Features Correlating Significantly ($p < .05$) with Diagnosis, in Order of Magnitude of Correlation and according to Diagnosis Suggested by Presence of Feature

Diagnosis	
Neurotic Depression	Endogenous Depression
Reactivity of depression	Early awakening
Precipitation	Depression worse in morning
Self pity	Quality of depression
Variability of illness	Retardation
Hysterical features	Duration one year or less
Hysterical features (immaturity)	Age 40 or above
Inadequacy	Depth of depression
Initial insomnia	Failure of concentration
Reactive depression	Weight loss 7 lbs. or more
Depression worse in evening	Previous attacks
Sudden onset	
Irritability	
Hypochondriasis	
Obsessionality	

DISCUSSION

The results reported in this paper indicate clearly that the group of depressive states consists of two separate entities conforming with those conditions known so long as "endogenous" depression and "neurotic or reactive" depression. A great deal of evidence exists which supports this conclusion and some of it is summarized and discussed below.

Genetic Studies

There is considerable agreement that a single dominant autosomal gene showing incomplete penetrance is an essential pre-requisite to the development of endogenous depression (Kallmann, 1954; Shields and Slater, 1960; Stenstedt, 1952). It is possible that incomplete penetrance may play some part in determining the mildness of so many cases of endogenous depression, a fact which accounts for much of the difficulty in differentiating them from neurotic depressions.

In neurotic depression the evidence suggests strongly that, as with intelligence, stature and personality traits, we are dealing with a graded phenomenon. Slater (1950) regards neurosis as a dimension along which variation may occur—"neurotics do not show the marks of pathological determinance, they are heterogeneous"—and points out that the genetic basis for such states must be multifactorial. Much of the work of Eysenck (1960) has been directed to the same end and provides strong support for this hypothesis.

It seems then that genetic distinctions have been established between the two types of depression, the one being a pathological variant, the other differing only quantitatively from the normal experience of sadness or gloom. Merrell (1951) suggests that the fact that heredity plays differing aetiological roles in these states might be of value in tackling the problems of differential diagnosis insofar as these may be reflected in "physically measurable differences between the normal and the abnormal". Some of the evidence summarized later in this paper suggests that in fact this may be the case. If the genetic basis for the two conditions differs it might be anticipated that they would show differing associations with other genetically determined

conditions. Parker *et al.* (1961) have made the as yet unsubstantiated claim that the incidence of the type O blood group is significantly greater in the manic depressives than in patients suffering from neurotic depression. They have also found the incidence of Rhesus factor E to be significantly greater in the neurotic depression group than in either manic depressives or in the general population.

Studies of previous personality and of symptomatology

In his elaborate study of manic depressive psychoses and of "reactive psychoses" most of which were equivalent to the more severe examples of neurotic depression referred to in this paper, Astrup *et al.* (1959) confess that differential diagnosis may be difficult and sometimes impossible. Nevertheless, they found that such features as ideas of guilt and inferiority and a positive family history favour the former diagnosis, and noted that such patients usually show a syntonetic and well integrated personality, being free from neurotic traits. In the reactive group the illness was often coloured by the patient's life experiences and personality traits, evidence of a neurotic or psychopathic personality being present in the majority. Kay (1959) reached similar conclusions after studying a group of depressed patients over the age of 60 years. When cases were selected that showed retardation, severe agitation, ideas of guilt or self depreciation, nihilistic or hypochondriacal delusions, positive correlations could be established with a history of stable personality, good physical health and relatively little stress at the onset. The morbidity risk for manic depressive illness in first degree relatives was $10 \text{ to } 12.7 \pm 2.1$ per cent. It was found that in these patients E.C.T. was the likeliest form of treatment to be selected. In the patients whose depressive illnesses lacked these clinical features, the pre-morbid personality tended to be unstable, and there was often a history of social difficulties or physical disease related to the onset. The risk of manic depressive illness in the first degree relatives was only $3.5 \text{ to } 5.7 \pm 1.4$ per cent. and E.C.T. was not generally indicated. Kay concludes that the latter group may be regarded as the neurotic depressions of old age.

Stenstedt (1959) in his study of 307 cases of involuntional melancholia also found that these fell into two sharply delimited groups, the one consisting of cases of manic depressive illness and the other of "exogenous depression" characterized by low genetic loading for manic depressive illness and an onset related to stress.

Using a symptom-sign inventory, Foulds (1960) found that 14 of the 86 items recorded, enabled him to distinguish between cases of neurotic and endogenous depression. In 20 patients under 60 years of age diagnosed as suffering from endogenous depression the mean score was 6.85 ($SD=2.56$) and in a similar group of patients with neurotic depression the mean score was 2.35 ($SD=2.94$) ($t=5.7$ $p < 0.01$). Agreement with the clinical diagnosis was obtained in 90 per cent. of the psychotic depressions and 80 per cent. of the neurotic depressions. The differentiating items included ideas of unworthiness and guilt, anxiety, agitation, suicidal ideas, hypochondriasis and retardation. Application of the scale to 20 cases over 60 years of age regarded initially as suffering from psychotic depression more because of their age than on phenomenological grounds, produced a bimodal distribution, 65 per cent. falling in the psychotic depressive range and 35 per cent. in the neurotic depressive range. The findings of these observers, Astrup, Stenstedt, Kay and Foulds, show a striking similarity, each achieving a cleavage in a group of depressed patients which corresponds closely to the classical distinction between endogenous and neurotic depressions.

Hamilton and White (1959) carried out a factor analysis on data obtained from 64 severely depressed patients using Hamilton's rating scale (1960). The first of the four factors obtained covered such clinical features as depressed mood, guilt, retardation, loss of insight, suicidal attempts and loss of interest. It proved to be correlated with a clinical diagnosis of retarded depression. The patients were divided into four groups depending on the presence or absence of precipitating factors—endogenous, doubtful endogenous, doubtful reactive and reactive. Significantly different mean scores were obtained for this first factor between the endogenous and reactive groups,

the intermediate groups obtaining intermediate scores. This finding suggests that the two conditions differ, but does not indicate if the difference is a qualitative or merely a quantitative one. When plotted in the form of a graph, the scores showed a normal distribution but with two humps. It was felt that it might have been more definitely bi-modal had the number of cases studied been larger.

Physiological responses and tests

Sedation threshold. Shagass and Jones (1958), using the well-known technique of measuring the sedation threshold, have shown that cases of endogenous depression have significantly lower sedation thresholds than those of neurotic depression even though agitation is marked. In a study of 141 cases of endogenous depression and 94 of neurotic depression, the distribution of the scores showed a very marked bi-modal distribution. Boudreau (1958) and Nymgaard (1959), using a modified technique, reached the same conclusion. Others, it must be confessed, notably Ackner and Pampiglione (1959) found the sedation threshold test impossible to validate. Roberts (1959b) too could find no significant difference between the groups, but he used slurring of speech as an index of the threshold, a method regarded by Shagass as unreliable. Even using the less precise "sleep threshold" which dispenses with the need for an electroencephalograph, Shagass and Kerenyi (1958) found the same significant bi-modal distribution of scores when 30 psychotic depressives and 28 neurotic depressives were studied, though Martin and Davies (1962) were unable to confirm this finding.

The cycle of cortical excitability following electrical stimulation of the ulnar nerve has been investigated by Shagass and Schwartz (1961, 1962). Neurotic patients, including those suffering from depression, showed no difference from normals, but in 21 patients with psychotic depression the mean recovery time was significantly increased. After successful treatment this returned to normal.

The Funkenstein Test has proved more difficult to apply and less reliable than the sedation threshold test, though Sloane *et al.* (1957) found

some indication of dichotomous results within a group of depressed patients. Roberts (1959b) failed to confirm Funkenstein's claims concerning the prognostic value of the test in cases of depression treated with E.C.T., though in a similar study by Hamilton and White (1960) the test results showed a correlation of $+0.26$ with outcome, a finding they regarded as being "disappointing, but suggesting that the test was worthy of further investigation".

Strongin and Hinsie (1939) developed a method of measuring the parotid secretion and found that if a secretion rate of 0.01 ml. per 5 minutes was taken as the dividing line, 23 of 25 cases of endogenous depression showed rates below this figure. Of 25 patients with other varieties of depressive states—these included some schizophrenics and organic disorders as well as examples of neurotic depression—the rate of salivary secretion was above this level in 24. Busfield *et al.* (1961) although finding no difference between cases of mild and severe depression, confirmed that the sub-division into exogenous and endogenous cases was correlated with significantly different rates of secretion, that for the endogenous examples being the lower.

The effects of methylamphetamine upon cases of depression have been shown by Roberts (1959b) to have diagnostic value and his findings suggest strongly that there is a qualitative difference between the endogenous and neurotic cases. The intravenous administration of 15 mg. methylamphetamine produced effects on mood, behaviour and symptoms. In all but two patients, either of two responses occurred, a "normalization" or an "intensification" of the symptoms.

	Neurotic Depression	Endogenous Depression	Unclassified
N (normalization) response	25	3	3
I (intensification)	1	16	0
Atypical response	2	0	0
Total	28	19	3

$\chi^2 = 26.8$, Df = 1, $p < .01$
(unclassified cases and those with a typical response omitted)

An earlier study by Monro and Conitzer (1950) though not so conclusive, showed rather similar results. Cases of depression were arranged in groups according to prognostic factors established as the result of giving E.C.T. The effect

of methylamphetamine was found to be poor, except in the final group, the members of which showed the highest number of unfavourable features, including duration of illness over one year, age over 60 years, and a poor previous personality with marked neurotic or psychopathic traits.

The work of Dawson also shows a dichotomy in a depressive material. Dawson, Hullin and Crocket (1956) demonstrated that the blood level of acetylmethylcarbinol (AMC), a breakdown product of pyruvic acid, was raised before and during the onset of a depressive phase in patients with manic depressive psychosis. Dawson (1960) and Anderson and Dawson (1962) studied 98 cases of depression aged under 65 years. A high fasting level of blood AMC showed a significant positive correlation with high scores for verbal retardation and preoccupation with ideas of guilt and self-blame. Such patients (type A depressions) tended to have higher scores on such features as general anxiety, specific or phobic anxiety, hypochondriasis, depersonalization, obsessive compulsive manifestations, and paranoid ideas. The high AMC level in these cases appeared to be related to Na⁺ retention. The remaining cases (type B depressions) in which biochemical changes were slight or absent, showed clinical features corresponding to neurotic depression. Dawson emphasized that though the dichotomy was evident, it tended in some respects to cut across the usual diagnostic categories. There was, however, a broad correspondence between type A and endogenous depression and between type B and neurotic depression.

Depressive syndromes and body build

Although it is commonly accepted that a pyknic or endomorphic body build is associated with a propensity to manic depressive psychosis, few attempts appear to have been made to establish links between indices of body build and discrete depressive syndromes. Rees (1944) demonstrated an association between anxiety, neurotic depression, obsessional symptoms and a leptomorphic physique, as compared with the euryomorphic association found in a group of manic depressives. The patients were all males. The mean age of the manic depressive group was

significantly higher than that of the neurotic patients, but it was felt that this could account for only part of the difference in physique. In a later study limited to females, Rees (1950) reached the same conclusions but admitted that the differences though significant were not sufficiently marked to be of diagnostic value or to have prognostic import. Hamilton and White (1960) measured the Rees-Eysenck body index in a group of 20 endogenous and 29 reactive male depressives. There was a correlation of $+0.29$ between an endomorphic body build and a successful outcome with E.C.T. Roberts (1959), using the same scale, also confirmed a tendency for an endomorphic physique to be associated with a better outcome after E.C.T., this trend being more evident at three months than at one month. The correlation coefficient between body index and symptom score was in fact 0.617 at one month and 0.767 at three months, both being significant at the $.001$ per cent. level.

Relationship of prognosis to the depressive syndromes

In discussing the prognosis of the affective disorders, Lewis (1950) suggests that this depends upon the balance between particular intrinsic and extrinsic causal factors. He goes on to suggest that a history of a definite affective psychosis in the parent or grandparent indicates a greater probability of recovery from the attack, the suggestion being, therefore, that when "intrinsic factors" are stronger, the prognosis is better. Milder forms of illness, a group heavily weighted with those cases regarded as neurotic depression in this paper, he admits tend to become more chronic. These would seem to be two paradoxes which, if true, are surely without parallel in medicine.

In his well-known prognostic study of melancholia, Lewis (1936) was unable to establish any consistent prognostic signs, and when the series of 61 patients was arranged in order of prognosis, no feature or combination of features clustered at either end. It is important to bear in mind that no statistical methods were used to examine the data, and more important perhaps that the study was made before convulsive therapy became available.

It is in regard to the effects of the physical treatments, that the dichotomous nature of

depressive states is most apparent. There is general agreement, much of it perhaps impressionistic, that cases of endogenous depression respond better to E.C.T. than those of neurotic depression. Some go farther and stress that E.C.T. may make these latter patients worse (Sargant, 1961). Kalinowsky (1959) suggests that the different response in these two types of depression may have diagnostic significance. Even when the treatment is beneficial in cases of neurotic depression, all too often its effects prove to be ephemeral (Kalinowsky, 1954). The series of cases described by Roth (1959) demonstrates the discrepant response with convincing clarity.

	Total	Symptom Free	Marked Improvement	Slight Improvement
Endogenous depression	64	45	12	7
Reactive depression	21	3	9	9

$$\chi^2 = 21.07, Df = 2, p < 0.01$$

If neurotic depression is merely a mild variety of endogenous depression, here then is a third extraordinary paradox to set alongside the two already indicated—that a mild condition fails to respond and may even be made worse by a form of treatment that is effective in severe varieties of the same condition!

Several investigations have been carried out to determine whether any of the clinical features which occur in cases suffering from depressive states have prognostic relationship to the outcome with E.C.T. Hobson (1953) recorded the presence or absence of 121 clinical items in each of 127 in-patients at the Maudsley Hospital. Features which proved to be significantly correlated with good outcome were sudden onset, good insight, obsessional personality, self-reproach and short duration. Those indicating a poor outcome were hypochondriasis, depersonalization, emotional lability, neurotic traits, hysterical attitude to symptoms, above average intelligence and a fluctuating course. Prediction of outcome of the illness based on these correlates proved successful in 79 per cent. of cases. It is interesting to note the similarity between Hobson's findings and those reported by Kiloh *et al.* (1962). At first sight a glaring exception would appear to be "sudden onset". In Hobson's material, however, onset was described as

sudden if the condition developed over a period of eight weeks. The two groups of clinical features show a reasonable correspondence to endogenous and neurotic depression respectively. It is interesting that Hobson himself gave no consideration to this possibility and in fact made no attempt to classify his patients in any way. It would doubtless be of interest to carry out a factor analysis on his data.

Roberts (1959a) investigated 50 women aged 40–60 years all suffering from depressive illnesses regarded as justifying treatment with E.C.T. Using Hamilton's rating scale for depression, symptom scores were obtained for each patient before, and one month and three months after, treatment. He confirmed that Hobson's clinical item score was of value in predicting outcome and also that patients with high initial symptom scores tended to respond better to treatment. The clinical item score (Hobson) of these patients showed a correlation of -0.495 (significant at .001 per cent. level) with the initial symptom scores. In other words, a high clinical item score tended to be associated with a low initial symptom score and therefore with a poor outcome to E.C.T. To obtain a high score on the clinical items (Hobson) a fairly large number of neurotic features must be present. As Roberts points out, it seems improbable, if the difference were merely a quantitative one, that marked neurotic traits would be so much more common in the less severely depressed patients. When the question of diagnosis was considered, it was found that none of the 20 patients with psychotic depression had a clinical item score (Hobson) over 5, whilst of the 27 cases regarded as suffering from neurotic depression, 20 had scores of 6 or more. Roberts concludes that this evidence strongly supports that there are in fact two qualitatively different groups of depressed patients; firstly, those characterized by low initial symptom scores on Hamilton's rating scale, a high incidence of neurotic features—and therefore a high clinical item score (Hobson)—and a tendency to do less well with E.C.T.; and secondly, a group in which the converse features are found. These correspond to neurotic and endogenous depression.

A paper which concludes there is no distinc-

tion between neurotic and endogenous depression, and which has exerted considerable influence, is that of Garmany (1958). Garmany groups his cases into the orthodox categories and his material consists of 295 cases of endogenous depression, 36 cases of involutional depression, and 194 cases of reactive depression. In each case he recorded whether constitutional loading (inferred from such factors as pyknic habitus, positive family history, and history of previous unprovoked attacks) or stress factors (including not only environmental stresses but "personal stress factors", in other words "those facets of personality structure which make living less easy but do not of themselves predispose to depression") were present. The age distributions were noted, and he also recorded the treatment recommended, including E.C.T. In regard to constitutional loading, the importance of stress factors and age distribution, Garmany believed there was no significant difference between the three diagnostic categories. This statement was entirely impressionistic, and, in fact, when his figures are subjected to statistical tests—even accepting his very loose and wide-flung definitions—there are significant differences between the groups of patients classified as endogenous and reactive depression in relation to each item.

	Endogenous Depression	Reactive Depression
Number	295	194
Notable constitutional loading ..	98	40
Not stated	5	17

$$\chi^2 = 6.616; Df = 1, p < 0.02$$

	Endogenous Depression	Reactive Depression
Number	295	194
Stress factors absent	64	11

$$\chi^2 = 23.14; Df = 1, p < 0.01$$

When χ^2 is calculated on the age group frequencies given by Garmany for the two categories it again shows a significant difference ($\chi^2 = 10.65; Df = 4; p < 0.05$).

In 109 of 295 cases of endogenous depression E.C.T. was advised whilst this same advice was tendered in only 9 of 194 patients with reactive depression. It was not known whether or not the cases in fact received this treatment and no

information was available concerning its outcome. Garmany concluded that the distinction between these three forms of depression and particularly that between endogenous and reactive varieties is an unreal one. If there is a fundamental distinction between the groups he believes it is only in regard to "the reactivity or the readiness with which the patient responds to the mood of the examiner". This quality he thinks "is used to determine the need for E.C.T., the risk of suicide and . . . the diagnosis". Lesser reactivity he equates with depth of depression—"this is different from saying depression is more endogenous". And yet as Roth (1959) has pointed out, it is a remarkable thing that when one uses the traditional division into endogenous and neurotic depression one finds that it correlates so highly with the choice of E.C.T. or psychotherapy. Moreover, as has been pointed out, closer scrutiny of Garmany's figures demonstrates further correlates between diagnosis, the amount of constitutional loading, the presence of stress factors, and age.

It is of interest to compare Garmany's figures with those obtained from a survey of mental illness in the North-East of England requiring in-patient treatment between 1957 and 1960. This demonstrates that the frequency of choice of E.C.T. and the response of those given this form of treatment show highly significant differences in the two forms of depressive illness.

	Endogenous Depression	Neurotic Depression
Total	1330	774
Treated with E.C.T.	1062 (79·8%)	359 (46·4%)
Symptom free after E.C.T.	513 (48·3%)	91 (25·3%)

Similar discrepant results have been found in relation to treatment by prefrontal leucotomy. Sargent (1961) emphasizes that the results of leucotomy are better in cases of reactive depression—that is in the patient who is nervous and tense and is thrown into depression by "difficulties in his internal or external life". In endogenous depression, although the attacks are usually modified, their periodicity may remain unaffected. The figures given by Partridge (1949) clearly show a differential effect. Symptoms persisted after operation in 20 of 61

cases of endogenous depression, but in none of 21 cases of reactive depression. Pippard's cases (1955) show the same trend, a good result being obtained in 10 of 15 cases of neurotic depression and in 10 of 30 patients suffering from endogenous depression. The difference however does not quite reach the level of statistical significance.

Elithorn (1959) found himself in agreement with Partridge and Pippard and concluded that his results support the view that "some endogenous depressions are prognostically and aetiologically distinct from most reactive depressions". The group of cases subjected to leucotomy is, of course, a very highly selected one, the great majority having been subjected to all other forms of treatment without avail.

The discrepant response of cases of endogenous depression and neurotic depression to imipramine have been referred to earlier. When cases were selected in which the diagnosis could be made with confidence, it was found that all but one of 15 cases of endogenous depression responded well to imipramine within four weeks and remained well after six months, whereas only 16 of 32 cases of neurotic depression were improved after four weeks and 5 of these had relapsed within six months. (At 4 weeks $\chi^2 = 6·54$; $p < 0·02$; at 6 months $\chi^2 = 11·99$; $p < 0·01$; Kiloh *et al.*, 1962). Ibor (1962) found that 51·2 per cent. of 125 patients suffering from depressive states responded to imipramine, but when cases of "vital depression"—that is, typical endogenous depression—were selected, the response rate was found to be 84·5 per cent. suggesting that the "vital" types of depression are much more responsive to pharmacological treatment. Similar findings have been achieved with other drugs. In an uncontrolled pilot study of the effects of a dibenzazepine compound (G.33 040) on a mixed group of depressions it was found that cases of endogenous depression did significantly better than cases of neurotic depression (Kiloh *et al.*, 1962).

	Endogenous Depression	Neurotic Depression
Total number of cases	28	34
Good result at 3 weeks	16 (57%)	8 (24%)
Good result at 3 months	12 (43%)	4 (12%)

3 weeks = $\chi^2 = 5·71$; Df = 1; $p < 0·02$
 3 mths. = $\chi^2 = 6·21$; Df = 1; $p < 0·02$

Harrington and Imlah (1960) reported comparable results following the use of phenelzine.

	Endogenous Depression	Neurotic Depression
Total number of cases	54	28
Recovered or much improved	38 (70%)	7 (25%)
Improved or no change	16 (30%)	21 (75%)

$$\chi^2 = 13.55; Df = 1; p < 0.01$$

CONCLUSIONS

This survey of the literature shows that a considerable number of studies have been carried out, each pointing to the same conclusion. Not all those quoted are equally valid or important, but together they constitute a mass of evidence consistent with and supporting the traditional dichotomy of depressive cases into neurotic and endogenous varieties—a division strongly supported by the findings reported in this paper.

There may once have been some justification for refusing to distinguish one depressive patient from another—pessimistic and unrealistic though this may have been. Now on the contrary there is every reason to make the distinction for the choice of treatment and the accurate assessment of prognosis is dependent upon it. Unfortunately, although the importance of the distinction has become more apparent over the years it has scarcely become any easier, dependent as we are on our fallible clinical methods.

The emphasis should now be on the greater refinement of these methods and on the development of objective tests which would aid the differentiation of those cases which for one reason or another show mixed features and are a source of such diagnostic difficulties.

ACKNOWLEDGMENTS

We are deeply indebted to Professor Martin Roth for his advice and encouragement. We are grateful to Dr. E. S. Page, Director of the Computing Laboratory, University of Durham, Miss E. D. Barraclough, computer operator, and Miss S. O. Allison for their help in processing the data.

REFERENCES

- ACKNER, B., and PAMPIGLIONE, G. (1959). *J. Psychosom. Res.*, **3**, 271.
- ASTRUP, C., FOSSUM, A., and HOLMBOE, R. (1959). *Acta Psychiat. Neurol. Scand.*, **34**, Supp. 135.
- ANDERSON, W. McC., and DAWSON, J. (1962). *J. ment. Sci.*, **108**, 80.
- BALL, J. R. B., and KILOH, L. G. (1959). *Brit. med. J.*, **2**, 1052.
- BOUDREAU, D. (1958). *Arch. Neurol. and Psychiat.*, **80**, 771.
- BURT, C. (1940). *The Factors of the Mind*. London: University of London Press.
- (1952). *Brit. J. Psychol. stat. Sect.*, **5**, 109.
- BUSFIELD, B. L., WECHSLER, H., and BARNUM, W. J. (1961). *Arch. gen. Psychiat.*, **5**, 472.
- CATTELL, R. B. (1943). *Psychol. Rev.*, **50**, 559.
- DAWSON, J. (1960). "Biochemistry of depression" in *Final Report on the Symposium on Depression*, held at Royal College of Surgeons, 24 May 1960, p. 24.
- HULLIN, R. P. and CROCKETT, B. M. (1956). *J. ment. Sci.*, **102**, 168.
- ELITHORN, A. (1959). *Proc. Roy. Soc. Med.*, **52**, 203.
- EYSENCK, H. J. (1960). "Classification and the problem of diagnosis" in *Handbook of Abnormal Psychology*, ed. Eysenck, H. J. London: Pitman.
- FISHER, R. A. (1941). *Statistical Methods for Research Workers*. 8th Ed. Edinburgh: Oliver & Boyd.
- FOULDS, G. A. (1960). *J. ment. Sci.*, **106**, 1394.
- GARMANY, G. (1958). *Brit. med. J.*, **2**, 341.
- HAMILTON, M. (1960). *J. Neurol. Neurol. Psychiat.*, **23**, 56.
- and WHITE, J. M. (1960). *J. ment. Sci.*, **106**, 1031.
- — (1959). *J. ment. Sci.*, **105**, 985.
- HARRINGTON, J. and IMLAH, N. W. (1960). "A preliminary evaluation of phenelzine in a neurosis unit" in *Final Report of the Symposium on Depression*, held at Royal College of Surgeons, 24 May 1960, p. 55.
- HOBSON, R. F. (1953). *J. Neurol. Neurosurg. and Psychiat.*, **16**, 275.
- IBOR, J. L. (1962). *Compr. Psychiat.*, **3**, 15.
- KALINOWSKY, L. B. (1954). "Some problems in electric convulsive therapy of depressions", in *Depression*, ed. Hoch, P. H. and Zubin, J. New York: Grune & Stratton. p. 190.
- (1959). *Canad. psychiat. Assoc. J.*, (Spec. Supplement) **4**, S, 138.
- KALLMANN, F. J. (1954). "Genetic principles in manic-depressive psychosis" in *Depression*, ed. Hoch, P. H. and Zubin, J. New York: Grune & Stratton. p. 1.
- KAY, D. (1959). *Proc. Roy. Soc. Med.*, **52**, 791.
- KILOH, L. G., and BALL, J. R. B. (1961). *Brit. med. J.*, **1**, 168.
- — and GARSIDE, R. F. (1962). *Brit. med. J.*, **1**, 1225.
- ROY, J. R., and CARNEY, M. W. P. (1963). *J. Neuro-psychiat.* In press.
- KRAINES, S. H. (1957). *Mental Depressions and their Treatment*. New York: Macmillan.
- LEWIS, A. J. (1934). *J. ment. Sci.*, **80**, 277.
- (1936). *J. ment. Sci.*, **82**, 488.
- (1929). *A Clinical and Historical Survey of Depressive States based on the Study of 61 Cases*. M. D. Thesis. University of Adelaide.
- (1950). Section XX, Psychological Medicine in *A Textbook of the Practice of Medicine*, ed. Price, F. W. London: Oxford University Press. 8th Ed., pps. 1924 and 1933.
- MAPOTHER, E. (1926). *Brit. med. J.*, **2**, 872.

- MARTIN, I., and DAVIES, B. M. (1962). *J. ment. Sci.*, **108**, 466.
- MERRELL, D. J. (1951). *Arch. Neurol. Psychiat.*, **66**, 272.
- MONRO, A. B., and CONITZER, H. (1950). *J. ment. Sci.*, **96**, 1037.
- NYMGAARD, K. (1959). *Arch. gen. Psychiat.*, **1**, 530.
- PARKER, J. B., THEILIE, A., and SPIELBERGER, C. D. (1961). *J. ment. Sci.*, **107**, 936.
- PARTRIDGE, M. (1949). *J. ment. Sci.*, **95**, 795.
- PIPPARD, J. (1955). *J. ment. Sci.*, **101**, 756.
- REES, W. L. (1944). *Proc. Roy. Soc. Med.*, **37**, 635.
- (1950). *J. ment. Sci.*, **96**, 426.
- ROBERTS, J. M. (1959a). *J. ment. Sci.*, **105**, 693.
- (1959b). *J. ment. Sci.*, **105**, 703.
- ROTH, M. (1959). *Canad. psychiat. Assoc. J.*, (Spec. Supplement), **4**, S. 32.
- (1960). *Compr. Psychiat.*, **1**, 135.
- SARGANT, W. (1961). *J. Neuropsychiat.*, **2**, Suppl. 1, S. 1.
- SHAGASS, C., and JONES, A. L. (1958). *Amer. J. Psychiat.*, **114**, 1002.
- SHAGASS, C., and KERENYI, A. (1958). *Canad. psychiat. Assoc. J.*, **3**, 101.
- and SCHWARTZ, M. (1961). Abstracts—3rd World Congress of Psychiatry, Montreal. Part 1, p. 76.
- (1962). *Arch. gen. Psychiat.*, **6**, 235.
- SLATER, E. (1950). "The genetical aspects of personality and neurosis" in *Congrès International de Psychiatrie*, Paris. VI: Psychiatrie sociale, p. 119.
- SHIELDS, J., and SLATER, E. (1960). "Heredity and psychological abnormality" in *Handbook of Abnormal Psychology*, ed. Eysenck, H. J. London: Pitman.
- SLOANE, R. B. (1961). *J. Neuropsychiat.*, (Suppl. No. 1), S. 11.
- LEWIS, D. J. and SLATER, P. (1957). *Arch. Neurol. and Psychiat.*, **77**, 540.
- STENSTEDT, Å. (1952). *Acta Psychiat. Neurolog. Scand.*, **27**, Supp. 79.
- (1959). *Acta Psychiat. Neurolog. Scand.*, **34**, Supp. 127.
- STRONGIN, E. I., and HINSIE, L. E. (1939). *Psychiat. Quart.*, **13**, 697.

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BJPpsych

The British Journal of Psychiatry

The Independence of Neurotic Depression and Endogenous Depression

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BJP 1963, 109:451-463.

Access the most recent version at DOI: [10.1192/bjp.109.461.451](https://doi.org/10.1192/bjp.109.461.451)

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